

# Targeting important unmet medical needs



Corporate Presentation

October 2021

# Forward-Looking Statements

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# Altamira Therapeutics at a Glance

Legacy programs provide potential opportunity to unlock value for investors in the medium-term via spinoff/divestiture

*Respiratory - Altamira Medica:*

- Bentrion<sup>™</sup> (AM-301) for protection against airborne viruses and allergens

*Neurotology - Auris Medical:*

- AM-125 for treating acute vertigo
- Sonuvi<sup>®</sup> (AM-111) for treating acute inner ear hearing loss
- Keyzilen<sup>®</sup> (AM-101) for treating acute inner ear tinnitus

**Transformative acquisition and merger in Summer 2021**

- Acquired Trasir Therapeutics (WU spinoff) and subsequently merged into Auris Medical

**Repositioning around RNA therapeutics**

- Trasir – pioneer in extrahepatic oligonucleotide delivery
- > 15 years of NIH funded research
- Versatile peptide-based OligoPhore<sup>™</sup> / SemaPhore<sup>™</sup> platform

**Initiated preclinical development of first RNA pipeline program off OligoPhore<sup>™</sup> platform**

- AM-401 for treatment of mutant KRAS-driven cancer

# Altamira Group



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Medical devices  
for protection against  
airborne allergens  
and viruses



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Therapeutics for  
inner ear disorders



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RNA therapeutics for  
extrahepatic targets

# Leadership Team



**Thomas Meyer | PhD**  
CEO and Chairman

Founder Auris Medical  
14 years with Disetronic Group  
incl. CEO and BoD member  
>20% sales CAGR  
\$3 bn market cap



**Samuel Wickline | MD**  
Chief Scientific Officer

Prof. of Cardiovascular Sciences,  
Molecular Physiology and Pharmacology,  
Medical Engineering at USF  
Former Prof. of Medicine, Physics,  
Biomedical Engineering, Cell Biology  
and Physiology at Wash U



**Elmar Schärli | CPA**  
Chief Financial Officer

~30 years private and  
public company  
finance and accounting  
experience in biotech  
and medtech



## Our Respiratory Business

- OTC nasal spray (AM-301; Bentrío™)
- Drug-free, preservative free medical device
- Protection against airborne viruses and allergens
- Launched in Europe (CE mark) in selected EU countries (Germany, Austria, France )
- FDA acceptance for Bentrío 510(k) application (allergy)
- Ramping up international sales through distributor network – eight Asian countries covered
- Addressing multibillion \$ markets



## Protects

as a physical barrier  
the nasal mucosa



## Traps

airborne particles through  
electrostatic effects



## Humidifies

the nasal mucosa and thus  
aids its functionality



## Protects for $\geq 3$ hours

Gel designed for extended  
nasal residence time

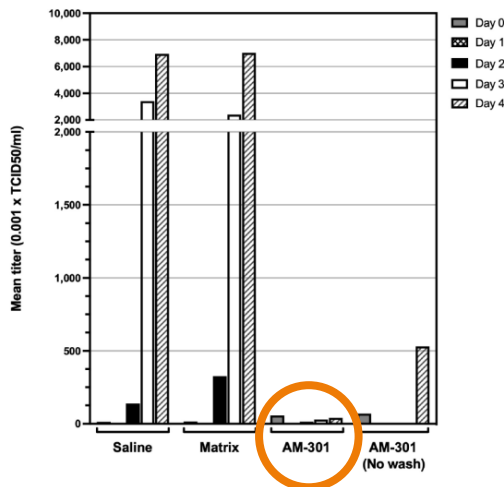


# Efficacy in SARS-CoV-2 and Influenza

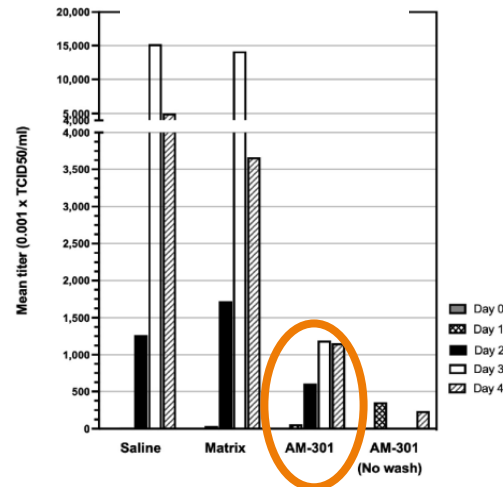
## Reconstituted human nasal epithelium model

- Functional nasal mucosa
- Without help from immune system or mucociliary clearance
- Median Tissue Culture Infectious Dose, TCID<sub>50</sub>, in Vero cells
- Daily treatment with Bentrio™

### Prevention Start 10' Before



### Mitigation Start 30 hrs After



## Highly effective protection

- >99% reduction in viral titer

## Activity also post infection

- Significant deceleration of viral titer growth

## New study showing significant protection also in influenza (H1N1), both with prophylaxis and treatment

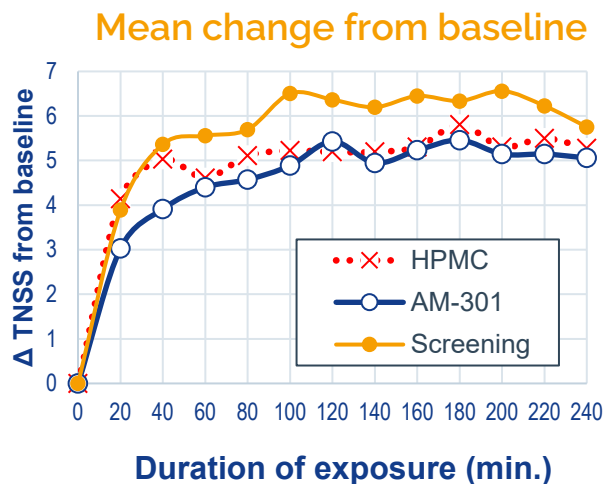
- Viral titer ↓ 84% and 77%



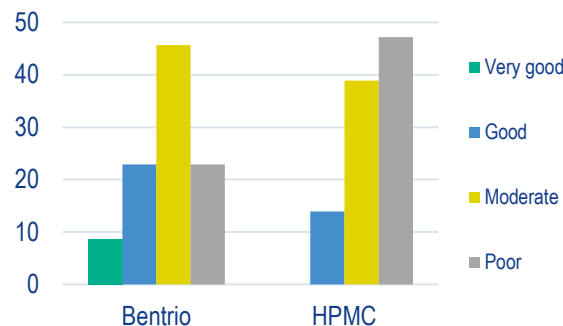
# Efficacy in Allergy

- Clinical pollen chamber study
- Open-label randomized cross-over study
- 36 patients with allergic rhinitis to grass pollen
- Single dose of Bentrio™ or HPMC powder spray prior to 4 hours of controlled pollen exposure

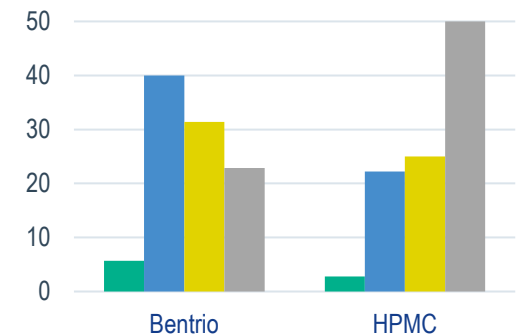
- Study met primary efficacy endpoint = substantial equivalence to predicate device for 510(k)
- Fast onset – significantly better at 20' and 40' timepoints
- Protective effect for 4 hours



Efficacy rated by subjects (%)



Efficacy rated by clinicians (%)



# Market Potential for Bentrío™

## Addressing Common Conditions

### Viral Infection

- Human rhinovirus (HRV) is most common cause of upper respiratory tract infection
- US revenues for cold and cough remedies: > \$12 billion in 2021<sup>1</sup>
- Influenza resulted in 9-45 million illnesses, 140,000-810,000 hospitalizations and 12,000-61,000 deaths annually since 2010<sup>2</sup>
- COVID-19: 174 million cases and 3.74 million deaths to date

<sup>1</sup> [www.statista.com](http://www.statista.com)

<sup>2</sup> Centers for Disease Control and Prevention

<sup>3</sup> Schiller et al., 2010

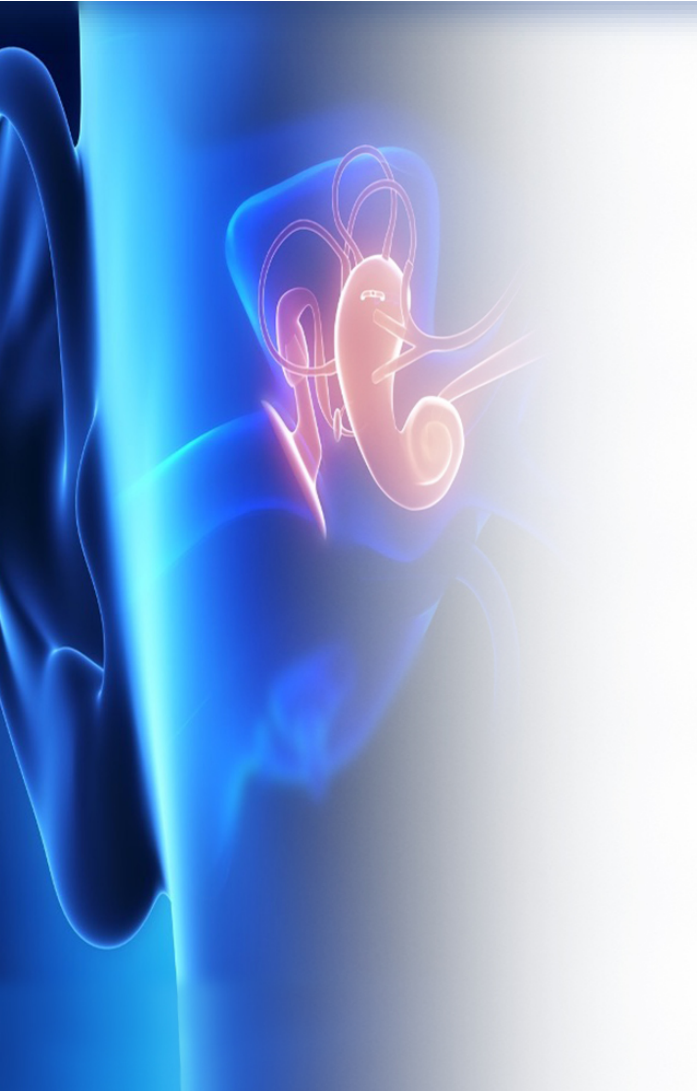
<sup>4</sup> [www.ibisworld.com](http://www.ibisworld.com)

<sup>5</sup> WHO

<sup>6</sup> Global Alliance on Health and Pollution

### Allergies

- About 7.8% of people 18 and over in the US have hay fever 11.1 million visits to physician offices with primary diagnosis allergic rhinitis<sup>3</sup>
- \$4 billion market size for OTC allergy medicines in US in 2020<sup>4</sup>
- Air pollution
  - > 90% of the world's population exposed to unhealthy air, 5th highest mortality risk factor globally<sup>5</sup>
  - E.g. causing 1.8 m premature deaths p.a. in China<sup>6</sup>



## Our Neurotology Business

- Rx nasal spray (AM-125)
- Reformulated betahistine for vertigo
- Superior bioavailability vs. oral form
- Global market size (oral, ex US) = \$450 mm
- Currently in Phase 2
- Phase 3 programs in hearing loss (AM-111) and tinnitus (AM-101) designated for partnering

# Intranasal Betahistine for Treating Vertigo

## AM-125 Acts as a Vestibular Stimulant

35.4% of the US population  $\geq 40$  years experience vestibular dysfunction<sup>1</sup>

Lifetime prevalence of vertigo interfering with daily activities is 3-8%<sup>2</sup>

**Betahistine – unique vestibular stimulant**

- World-wide SOC, but no longer marketed in US
- Current worldwide annual sales ~\$450 million<sup>3</sup>

**Rx options in US essentially limited to vestibular suppressants**

**AM-125 addresses betahistine's weak point = poor oral bioavailability (~1%)**

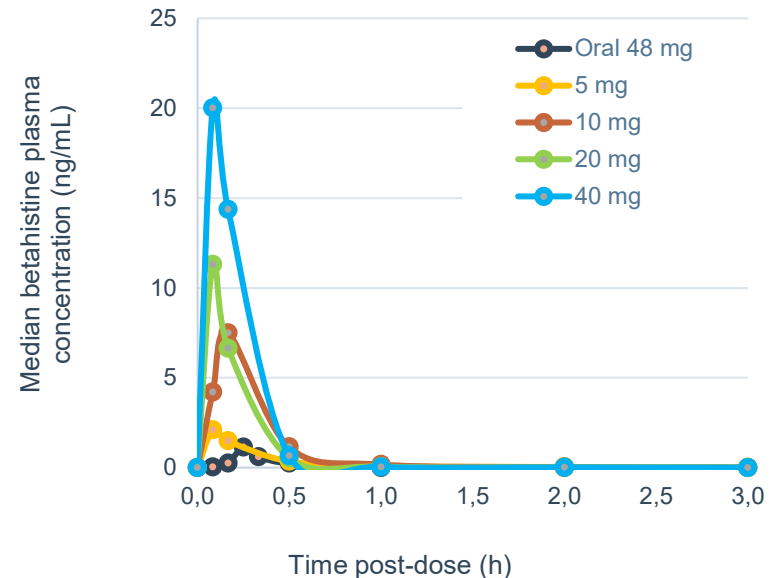
- Capture part of existing oral betahistine market
- Bring betahistine back to US

<sup>1</sup> Agrawal et al., 2009

<sup>2</sup> Mordin et al., 2015

<sup>3</sup> Oral betahistine, manufacturer prices (IMS).

## Superior Bioavailability Using Intranasal Route



- Betahistine targets the histaminergic system
- Increases inner ear and cerebral blood flow
- Increases histamine turnover and enhances histamine release in CNS
- Enhances release of acetylcholine, dopamine and norepinephrine in CNS
- Relative bioavailability of AM-125 vs. oral betahistine (daily dose) = 5 to 29 x

# AM-125 Development & Milestones

## Development Plan

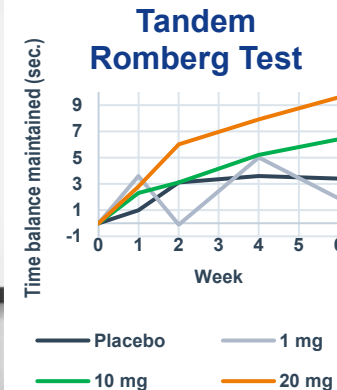
### Target indication and patient benefit

- Treatment of acute peripheral vertigo
- Enhance vestibular function
- Improve and accelerate vestibular compensation
- Get patients back on their feet asap!

### Clinical Milestones

- First Ph1 trial in 40 healthy volunteers (2015)
- Second Ph1 trial in 72 healthy volunteers (2018)
  - Both showing significantly higher bioavailability vs. oral delivery
- Treatment safe and well tolerated (maximum 40 mg t.i.d.)
- Ph2 trial in 118 acute vertigo patients (ongoing)
  - Acute vertigo following neurosurgery
  - Treatment for 4 weeks, 2-week treatment-free follow-up
  - Battery of balance tests + HRQOL questionnaires

## Recent and Upcoming Milestones



*Interim results from TRAVERS Phase 2 trial Part A in 31 patients suffering from acute vertigo following neurosurgery, treated t.i.d. for four weeks*

- Part A: dose dependent improvement in balance + other outcomes
- Continuing with 10 and 20 mg t.i.d. in Part B
- Data read-out in Q1 2022
- IND and start Phase 3 in H1 2022

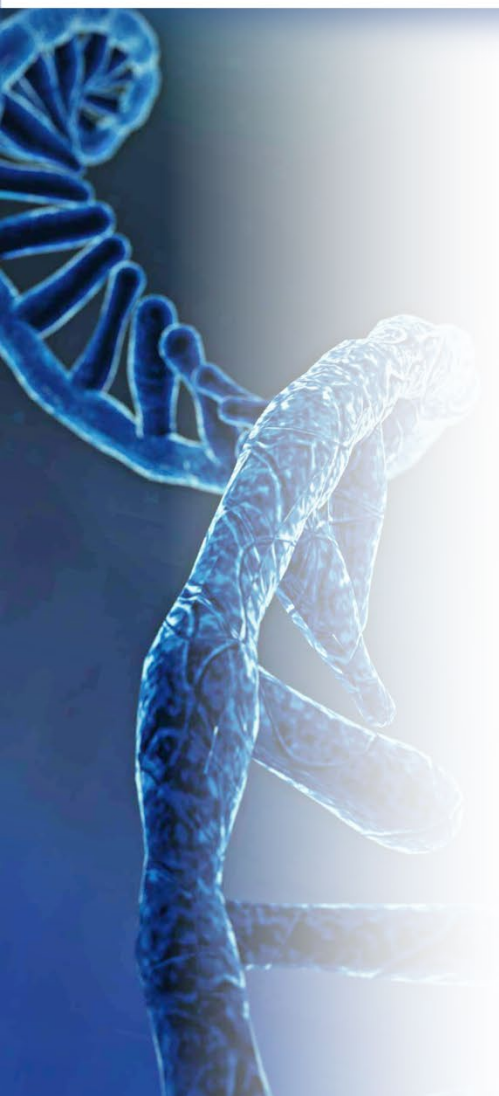
# Sonsuvi® (AM-111) and Keyzilen® (AM-101)

## Sonsuvi® in Acute Inner Ear Hearing Loss

- Prevents or attenuates hearing loss by protecting hair cell functionality
- Cell-penetrating peptide (brimapitide; JNK inhibitor )
- Single dose by intratympanic injection
- Orphan Drug (FDA and EMA), Fast Track (FDA)
- Phase 3 trial demonstrated significant and clinically relevant improvement in hearing recovery in acute profound hearing loss
- Second Phase 3 trial planned, incorporating regulatory feedback

## Keyzilen® in Acute Inner Ear Tinnitus

- Attenuates tinnitus intensity by blocking aberrant excitation of NMDA receptors
- Small molecule (esketamine; NMDA receptor antagonist)
- Three doses by intratympanic injection
- Fast Track
- Two positive Ph2 trials
- Failed to meet endpoints in Ph3 primarily due to design issues
- Ph 2/3 trial planned, incorporating regulatory feedback and learnings from previous trials



## We aim to become the leading company for extrahepatic RNA therapeutics

- Versatile peptide-based platform
  - OligoPhore™ (siRNA Payloads)
  - SemaPhore™ (mRNA Payloads)
- KRAS-driven cancer selected as first therapeutic indication for OligoPhore™ platform
- Exploring further potential applications



## Select Companies in RNA Therapeutics Space

Company	Ticker	Market Cap (mm) *	Indication	Phase
RNA Therapeutics				
Alnylam Pharmaceuticals, Inc.	ALNY	\$23,604	Hereditary ATTR, Acute Hepatic Porphyria	Commercial
Arrowhead Pharmaceuticals, Inc.	ARWR	\$6,884	Renal Cell Carcinoma	Ph1/2
Ionis Pharmaceuticals, Inc.	IONS	\$4,297	ATTR Amyloidosis, FCS, ALS	Ph3
PTC Therapeutics, Inc.	PTCT	\$2,541	Aromatic L-amino acid decarboxylase deficiency	Ph3/Commercial
Dicerna Pharmaceuticals, Inc.	DRNA	\$1,697	Primary Hyperoxaluria	Ph3
Translate Bio, Inc.	<i>Acquired</i>	\$3,200	CF	Ph1/2
Arcturus Therapeutics Holdings Inc.	ARCT	\$1,172	Ornithine Transcarbamylase Deficiency	Ph2
Arbutus Biopharma Corporation	ABUS	\$548	Hepatitis B Virus	Ph1a/1b

\* Data from Yahoo Finance as of 10/22/21

# Current Challenges

## In Nucleic Acid Delivery

Current state-of-the-art for delivery of nucleic acid therapeutics

- Viral-based vectors
- Pioneer in extrahepatic oligonucleotide delivery
- Lipid nanoparticles (LNPs)
- Ligand conjugates

Delivery technologies remain a key rate-limiting step for unlocking the potential of RNA therapeutics:

- Viral based delivery vectors suffer from lack of transduction efficiency and target specificity
- LNPs and currently available ligand conjugates using GalNac technology preferentially target the liver, and many have suboptimal

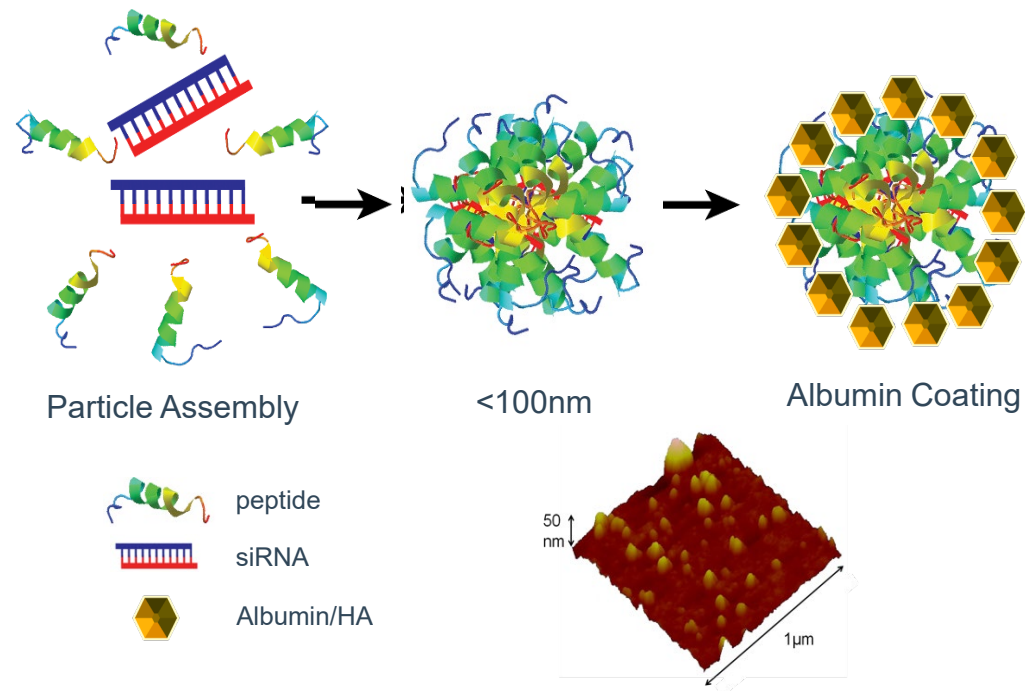
## How OligoPhore™ with siRNA Payloads SemaPhore™ with mRNA Payloads Work

The peptide-based OligoPhore™ / SemaPhore™ technology allows for safe and effective delivery of RNA payloads with systemic administration:

- *Stability*: RNA complexed in nanoparticle format for, and only released inside of cells after uptake
- *Extrahepatic delivery*: not sequestered in liver, but permeates inflamed pathological tissues
- *Endosomal escape*: pH-dependent nanoparticle disassembly, followed by full release of RNA into cytoplasm
- *Selectivity*: silences molecular targets in diseased tissues only
- *Safety*: no cellular or adaptive immune responsivity to nanoparticle components or RNA after multiple serial doses, and no organ toxicities in mice

*Phore* = Greek for agent, bearer  
*Sema* = Greek for sign, message

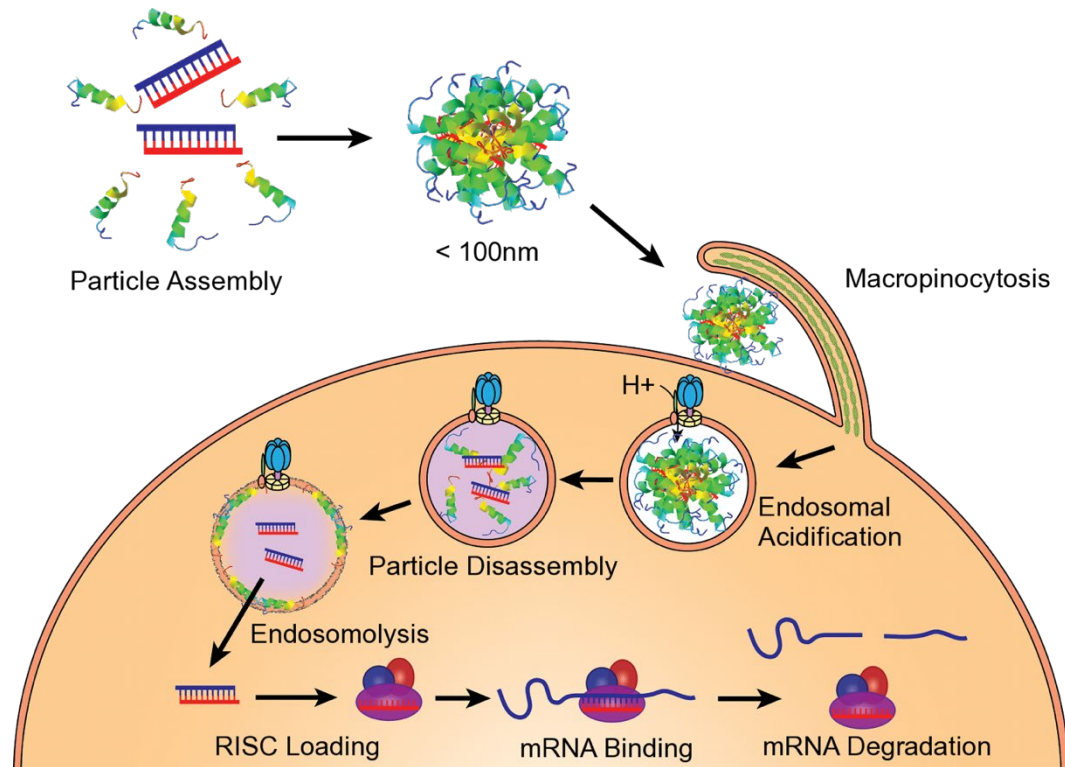
# Stable Peptide-siRNA Polyplex Formulation



Hou KK et al. Melittin derived peptides for nanoparticle-based siRNA transfection. Biomaterials. 2013;34:3110-9.

Hou KK et al. Mechanisms of nanoparticle-mediated siRNA transfection by melittin-derived peptides. ACS Nano. 2013;7:8605-15.

## Summary of OligoPhore™ Mechanism of Action



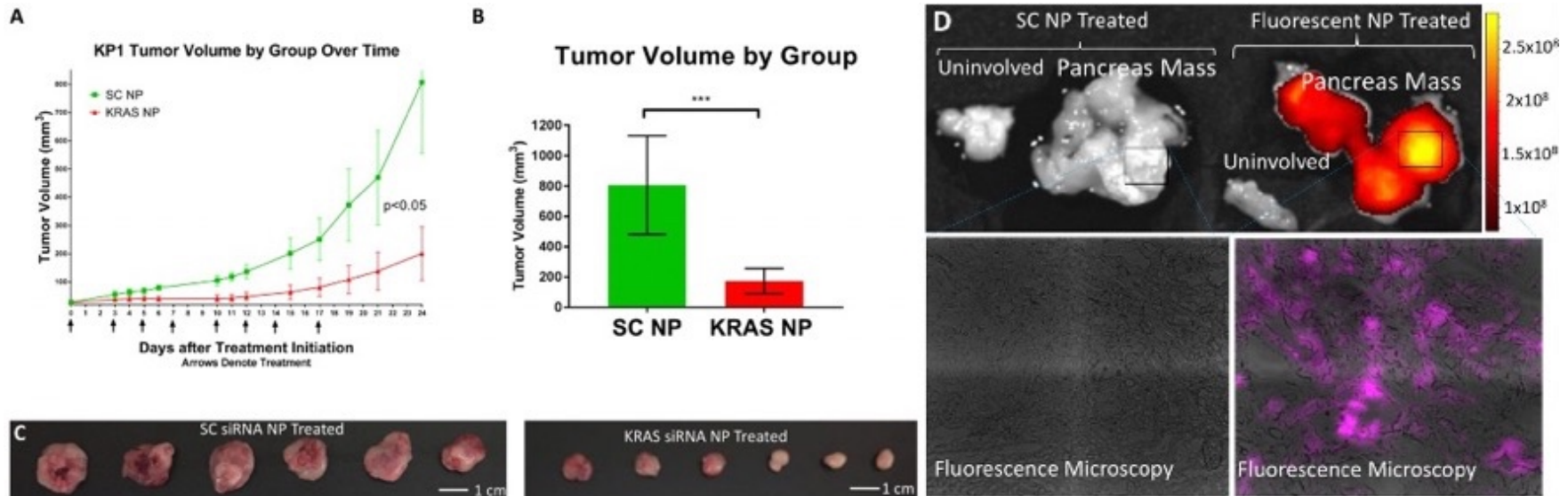
Hou KK et al. A role for peptides in overcoming endosomal entrapment in siRNA delivery - A focus on melittin. *Biotechnol. Adv.* 2015; 33(6 Pt 1): 931-40.

## Preclinical Data From 13 Murine Disease Models So Far

OligoPhore™ with siRNA Payloads

- Pancreatic and colorectal cancer (KRAS)
- Ovarian cancer (TAM: AXL)
- Lung cancer (ETV-2)
- Metastatic Melanoma (NFkB)
- Adult T Cell Leukemia / Lymphoma (NFkB)
- Sarcoma (MYCT-1)
- Necrotizing enterocolitis (NFkB)
- Rheumatoid and osteoarthritis (NFkB)
- Atherosclerosis (JNK2)
- Metabolic syndrome/Obesity (ASXL2)
- Aortic Aneurysm (NFkB)

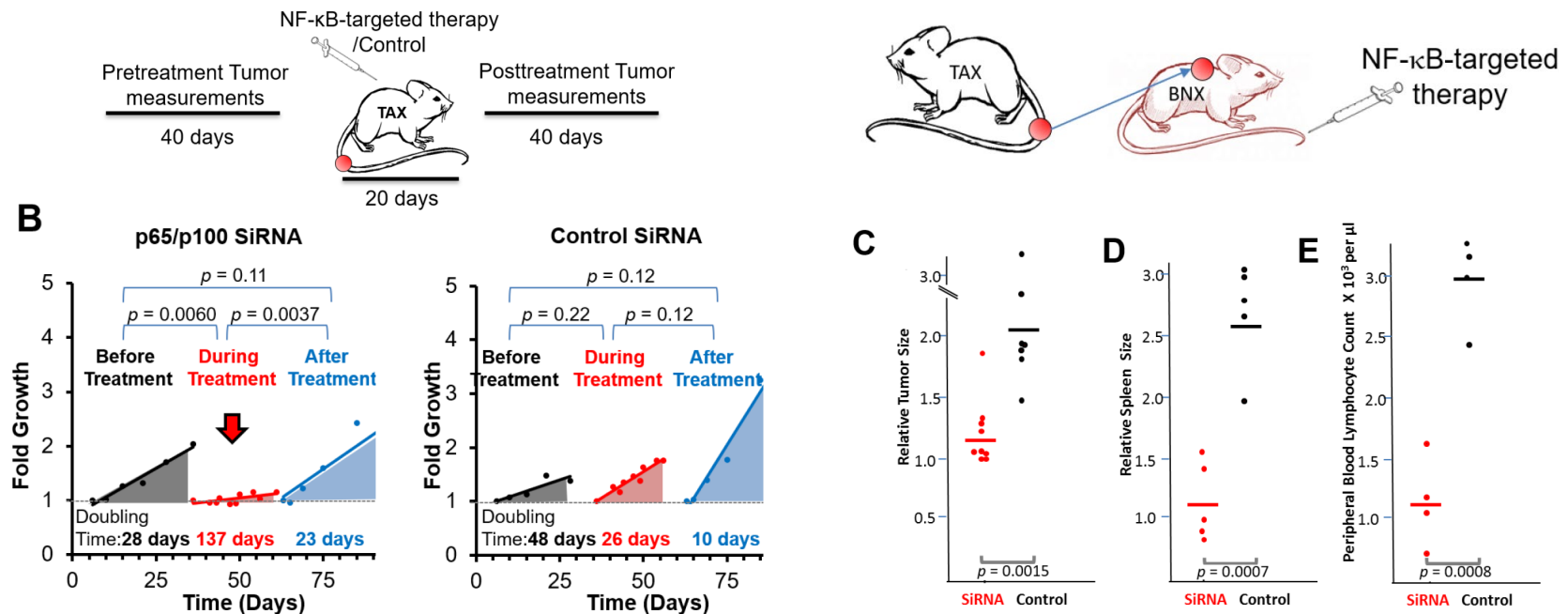
# Pancreatic Tumor Inhibition With KRAS siRNA



Strand MS et al. Precision delivery of RAS-inhibiting siRNA to KRAS driven cancer via peptide-based nanoparticles.  
Oncotarget. 2019;10:4761-4775.



# Tumor Growth Inhibition In Adult T-cell Leukemia / Lymphoma by NF- $\kappa$ B siRNA



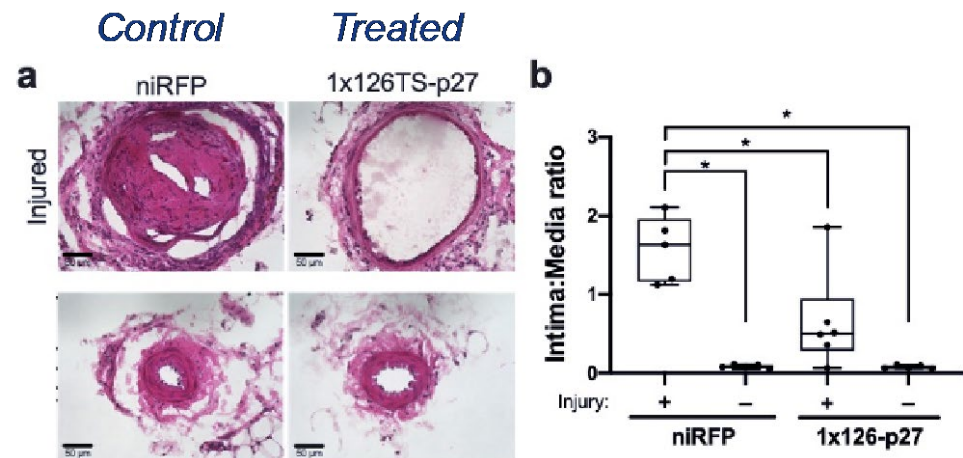
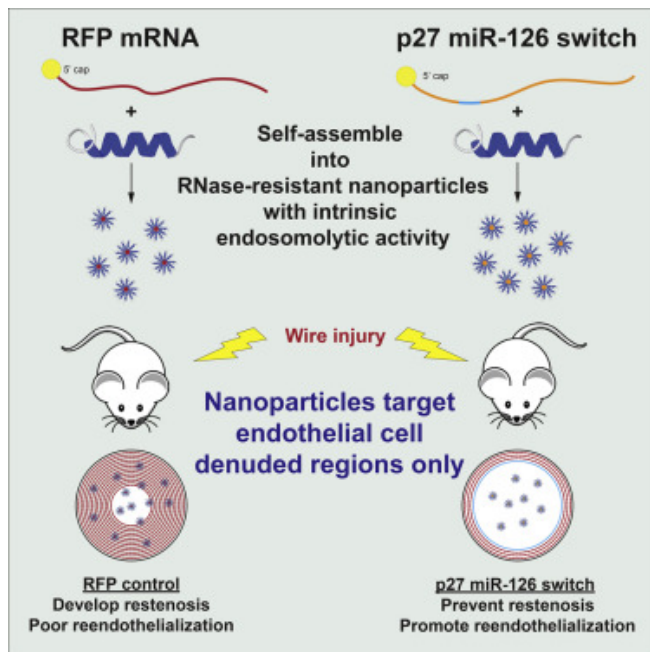
Rauch DA et al. Targeting NF- $\kappa$ B with nanotherapy in a mouse model of adult T-cell leukemia/lymphoma. *Nanomaterials* 2021, 11(6), 1582.

# Preclinical Data From 3 Murine Disease Models So Far

- Osteoarthritis (WNT16)
- Atherosclerosis (p27Kip1)
- Aortic Aneurysm (SOD2)

SemaPhore™ with mRNA  
Payloads

# Effective Treatment of Atherosclerosis by p27<sup>Kip1</sup> mRNA



Lockhart et al. Self-assembled miRNA-switch nanoparticles target denuded regions and prevent restenosis. Mol Ther. 2021; 5;29(5):1744-57.

# RNA Development Plan

- Initial focus on siRNA and existing data, while advancing research on mRNA and other payloads
- CMC upscaling and safety package incl. NHP tox study → targeting IND submission by end of 2022
- Team of in-house experts, complemented by network of consultants and CROs in EU and US
- Seeking to explore further therapeutic indications

# Multiple Potential Near- and Mid-term Value Inflection Points

Timeline	Q4 2021	Q1 2022	Q4 2022
<b>Respiratory (Bentrio™)*</b>		510(k) for allergy	
<b>Neurotology (AM-125)*</b>	Ph2 recruitment completed	Read-out Ph2	
<b>RNA Therapeutics (AM-401)</b>		Pre-IND studies	IND submission

\*Exploring opportunities to spinoff / divest respiratory and neurotology assets

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